REMARKS

Amendments

Claim 1 is amended above to clarify the language thereof and to include a "wherein" clause which further defines the claimed genus of compounds. In addition, the definition of group Z is amended to exclude fluorine substituents. Claims 2, 3 and 6 are amended to clarify the language thereof so as to use language in accordance with conventional U.S. practice. Claim 4 and use claim 7 have been canceled without prejudice. Use claims 8-11 have been amended to be in the format of method of treatment claims and further to use language in accordance with conventional U.S. practice.

New claim 14 is directed to a pharmaceutical composition. Method claim 15 is directed to subject matter previously recited in claim 9. Method claim 16 is directed to subject matter previously recited in claim 10. Further, method claims 17-18 are directed to subject matter previously recited in claim 11.

New claim 19 is directed to specific compounds. These compounds are described in Examples 32-38 of applicants' specification.

New claims 20-28 are directed to further aspects of the invention. Support is provided at, for example, pages 6-8, and the compounds described in the Examples.

Election

Applicants' hereby affirm the election of group I, claims 1-11. It is respectfully submitted that new claims 14-28 should also be included within the elected group.

Rejection Under 35 U.S.C. §101

Claims 7-11 are rejected under 35 U.S.C. §101 on the grounds that they are directed to nonstatutory subject matter, i.e., they are in the form of "use"claims. By the above amendment, applicants' have canceled claim 7 and converted claims 8-11 into method of treatment claims. Withdrawal of the rejection under 35 U.S.C. §101 is respectfully requested.

Rejection Under 35 U.S.C. §112, 2nd Paragraph

In the text bridging pages 5-6 of the Office Action, it is asserted that "claims", without identifying which claims, are rejected under §112, 2nd paragraph, as allegedly being indefinite. At the end of the text, it is stated that the "following reasons apply". However, the rejection does not provide any such reasons nor does it refer to any particular claim language as being indefinite. Withdrawal of the rejection under 35 U.S.C. §112, 2nd paragraph, is respectfully requested.

Rejection Under 35 U.S.C. §102(b) In View of Kirsh et al. (WO 97/00242)

Claims 1 and 4 are rejected under 35 U.S.C. §102(b) as being anticipated in view of Kirsch et al. (WO '242). This rejection is respectfully traversed.

Applicants' wish to inform the Examiner that there is a U.S. National Phase corresponding to WO '242, i.e., Serial No. 08/981,819 (filing date March 31, 1998). A Notice of Allowance and Issue Fee due was issued in Serial No. '819 on December 12, 2000. A continuation application of Serial No. '819 was filed on December 18, 2000, i.e., Serial No. 09/738,286.

In the rejection, reference is made to compounds 106a and 106b at page 2 of WO '242 and Example XXXIV at page 36. It is stated in the rejection that these compounds exhibit a cyclopropyl group at the C-25 position.

Compounds 106a and 106b, in addition to exhibiting the cyclopropyl group at the C-25 position, exhibit a keto group at the C-24 position. Also, Group Z, which is attached to the C-25 position, is CHOH-C_4F_9.

The compound of formula XXXIV at page 36 also exhibits a cyclopropyl group at the C-25 position and at the C-24 position exhibits the group $CHOR_{11}$. In addition, Group Z' is attached to the C-25 position. R_{11} is an acid-labile protective group having a definition analogous to Y'_1 or Y'_2, or is tetrahydropyranyl, tetrahydrofuranyl, ethoxyethyl, methoxymethyl, or methoxyethoxyethyl. See the disclosure at the middle of page 27. Y'_1 is a hydrogen atom or a protective hydroxy group and Y'_2 is a hydroxy protective group. See the description of Y'_1 and Y'_2 at page 22 immediately following formula II. Z' is analogous to group Z of WO '242 or optionally exhibits protective group-carrying substituents. See the bottom of page 22.

Compounds 106a, 106b and the compound of Example XXXIV of WO '242 fail to anticipate applicants' claim 1. See the "wherein" clause at the end of claim 1, which further defines Group Q (the C-24 position). See also the description of group Z which is attached to the C-25 position. Withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

Rejection Under 35 U.S.C. §103 In View of Kirsch et al. (WO '242)

Claims 1-11 are rejected as being obvious in view of Kirsch et al. In the rejection, reference is made to formula I at page 1 and Example XXXIV at page 36. Further, it is argued that WO '242 discloses 3-7 numbered carbocyclic or heterocyclic ring groups at the C-25 position.

In formula I of WO '242, the C-24 position is substituted by Groups A and B. Groups A and B can together form a keto group. Alternatively, Group A can be OR' and B can be a

hydrogen atom or B can be OR' and A can be a hydrogen atom. R' is a hydrogen atom, an alkanoyl group of up to 9 carbon atoms, or an aroyl group.

In the §102(b) rejection, only three specific compounds of WO '242 are mentioned. In compounds 106a and 106b, the C-24 position is substituted by a keto group. In the compound of Example XXXIV, the C-24 position is $CHOR_{11}$. The disclosure of WO '242 describes a broad genus of compounds. Within the genus, the substituent at the C-25 position is not specifically a cyclopropyl ring, but is instead a broader class of substituents as is acknowledged in rejection.

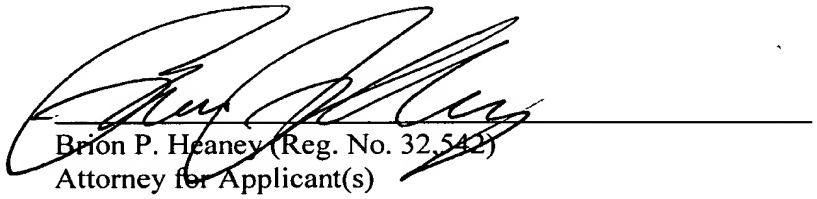
One of ordinary skill in the art presented with the disclosure of WO '242 and its broad genus of compound is not provided with sufficient motivation to modify the compounds therein, or particularly compounds 106a, 106b and the compound of formula XXXIV, in such a manner as to arrive at a compound in accordance with applicants' claims genus. The mere disclosure of a broad genus of compounds does not, in and of itself, establish obviousness with respect to each and every compound encompassed therein. See, for example, *In re Jones*, 21 USPQ 2d 1941 (Fed. Cir. 1991) and *In re Baird*, 29 USPQ 2d 1550 (Fed. Cir. 1994). Instead, the disclosure must provide some motivation which would lead one of ordinary skill in the art, without the benefit of hindsight, to modify the disclosed compounds in such a manner as to arrive at the claimed compound.

In this case, no such motivation is presented in WO '242 or is asserted in the rejection that would lead one of ordinary skill in the art to modify the C-25 cyclopropyl compounds disclosed in WO '242 in such a manner as to arrive at a compound in accordance with applicants' claimed genus. This is particularly the case for the compound of formula XXXIV which is described in WO '242 as an intermediate within a synthesis process. There is no motivation to interrupt the synthesis process, isolate the intermediate, and modify its structure. See, e.g., *In re Lalu et al.*, 223 USPQ 1257 (Fed. Cir. 1984).

In view of the above remarks, it is respectfully submitted that Kirsch et al. (WO '242) fails to provide sufficient motivation to render obvious applicants' claimed invention. Withdrawal the rejection under 35 U.S.C. §103 is respectfully requested.

Attached hereto is a marked-up version of the changes made to claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Respectfully submitted,



Brion P. Heaney (Reg. No. 32,542)
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
Arlington Courthouse Plaza I, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
(703) 812-5308 [Direct Dial]
(703) 243-6410 [Facsimile]
Internet Address: heaney@mwzb.com

Filed: **March 12, 2001**

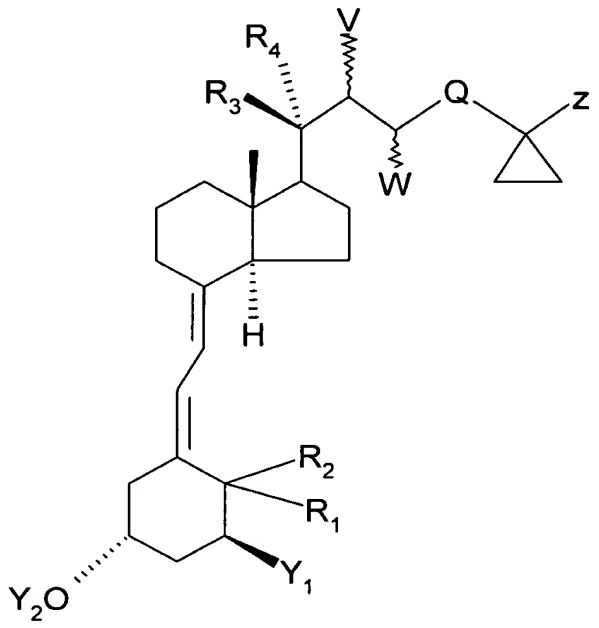
BPH:imm\K:\PAT\Sch\1747\Amendment 3-12-01.wpd

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Please cancel claims 4 and 7 without prejudice.

1. (Amended) A vitamin ~~Vitamin~~ D ~~derivatives~~ compound of ~~general~~ formula I,



in which

Y_1 means a hydrogen atom, a hydroxyl group, a fluorine, chlorine or bromine atom or a group $-OCOR_8$, in which

R_8 is an aliphatic or aromatic radical with 1 to 12 C atoms,

Y_2 means a hydrogen atom or a group $-(CO)R_9$, in which

R_9 is an aliphatic or aromatic radical with 1 to 12 C atoms,

R_1 and R_2 each mean a hydrogen atom or together an exocyclic methylene group,

R_3 and R_4, independently of one another, mean a hydrogen atom, a chlorine or fluorine atom, an alkyl group with 1 to 4 carbon atoms, or together form a methylene group or together with quaternary carbon atom 20 form a 3- to 7-membered, saturated or unsaturated carbocyclic ring,

V and W together mean an E-double bond or V means a hydroxyl group and W means a hydrogen atom,

Q means a straight-chain or branched carbon unit with up to 10 carbon atoms, which at any position can have α- or β-hydroxyl groups, which in turn can be etherified or esterified, keto groups, amino groups or halogen atoms,

Z means a straight-chain or branched-chain, saturated or unsaturated hydrocarbon radical with up to 12 carbon atoms, which at any positions can have keto groups, α- or β-hydroxyl groups, which in turn can be etherified or esterified, amino groups, ~~fluorine,~~ chlorine, or bromine atoms

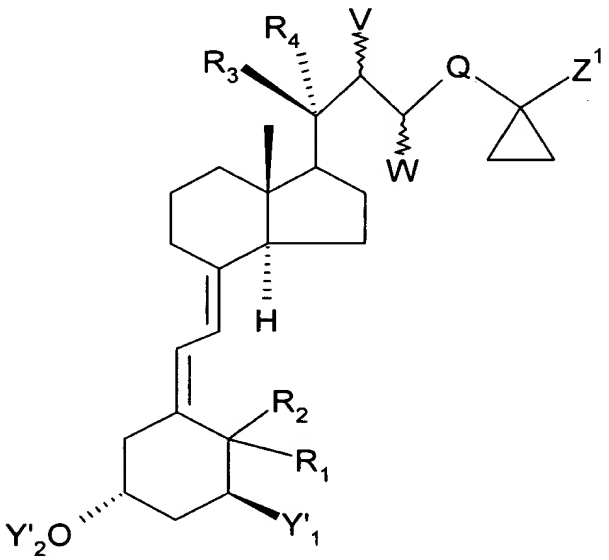
wherein Q is not -CHOH-.

2. (Amended) A compound ~~Vitamin D derivatives of general formula I~~ according to claim 1, wherein ~~in which~~ Q means an unsubstituted, unbranched alkylene unit with 1 or 2 carbon atoms, and Z means a straight-chain 1-oxoalkyl radical.

3. (Amended) A compound ~~Vitamin D derivatives of general formula I~~ according to claim 1, wherein ~~in which~~ Q means a -CH(OH)-CH_2-CH_2 radical, and Z means a straight-chain 1-oxoalkyl radical.

6. (Amended) A process ~~Process~~ for the production of compounds according to claim 1, ~~Vitamin D derivatives of general formula I, whereby~~ comprising:

converting a compound of ~~general~~ formula II



(II)

in which

Y'_1 means a hydrogen atom, a halogen atom, or a protected hydroxyl group and Y'_2 means a hydroxy protective group, ~~is converted~~

into ~~the~~ a compound of ~~general~~ formula I by simultaneous or successive cleavage of the hydroxy and keto protective groups and optionally by partial or complete esterification of free hydroxyl groups.

Please cancel claims 4 and 7, without prejudice.

8. (Amended) A method for treating a patient suffering from ~~Use of the vitamin D derivatives of general formula I according to claim 7 for the production of pharmaceutical agents for the therapy of~~ hyperproliferative diseases of the skin, pruritus, tumor diseases, precancerous stages, disorders of the immune system, inflammatory diseases, rheumatoid arthritis, asthma, auto-immune diseases, multiple sclerosis, diabetes mellitus, AIDS, or ~~as well as~~ rejection reactions ~~in the case of~~ associated with autologous, allogeneic or xenogeneic transplants comprising administering to said patient an effective amount of a compound according to claim 1.

9. (Amended) A method ~~Use~~ according to claim 8, wherein ~~the pharmaceutical agent also~~ said compound is administered in combination ~~combined~~ with other substances that have an immunosuppressive action~~, such as cyclosporin A, FK 506, rapamycin and anti-CD 4 antibodies~~.

10. (Amended) A method for treating a patient suffering from ~~Use of the vitamin D derivatives of general formula I according to claim 7 for the production of pharmaceutical agents for the therapy of~~ atrophic skin, ~~or~~ wounds ~~healing~~, ~~the therapy of~~ secondary hyperparathyroidism, renal osteodystrophia, ~~as well as~~ senile and postmenopausal osteoporosis, diabetes mellitus type II, ~~and the therapy of~~ or degenerative diseases of the peripheral and central nervous system ~~as well as the regulation of hair growth~~ comprising administering to said patient an effective amount of a compound according to claim 1.

11. (Amended) A method for treating a patient suffering from ~~Use of vitamin D derivatives of general formula I according to claim 7, which antagonize the action of calcitriol in HL 60 cells, for the therapy of~~ hypercalcemias or granulomatous diseases, ~~of~~ paraneoplastic hypercalcemias, ~~of~~ hypercalcemia in the case of hyperparathyroidism, ~~for male and female birth control or as immunostimulants, as well as in~~ hirsutism, ~~for the therapy and prophylaxis of~~ arteriosclerosis, ~~and~~

~~for the therapy of~~ or inflammatory diseases comprising administering to said patient an effective amount of a compound according to claim 1.